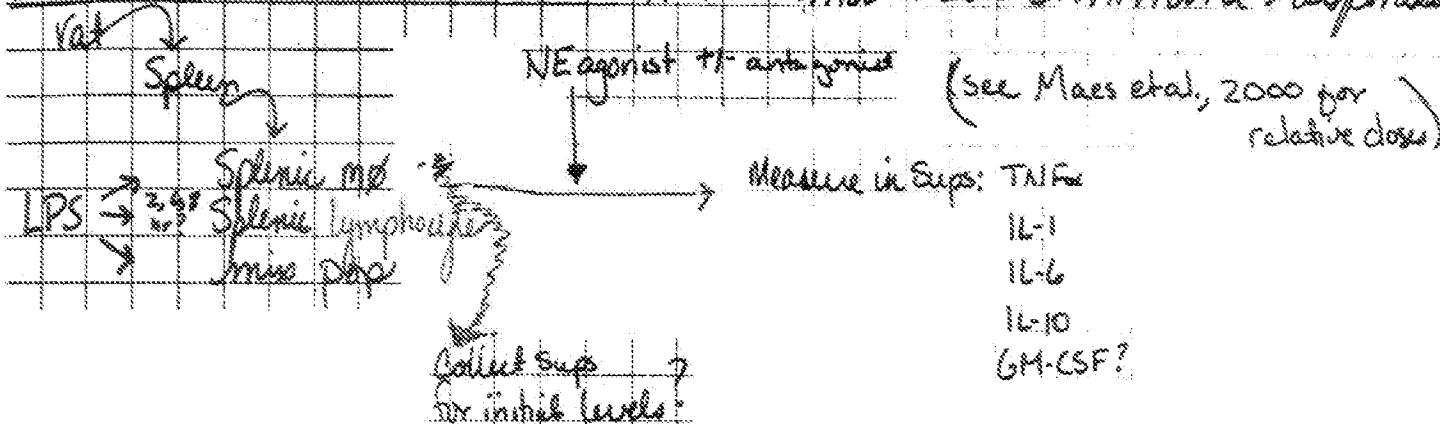


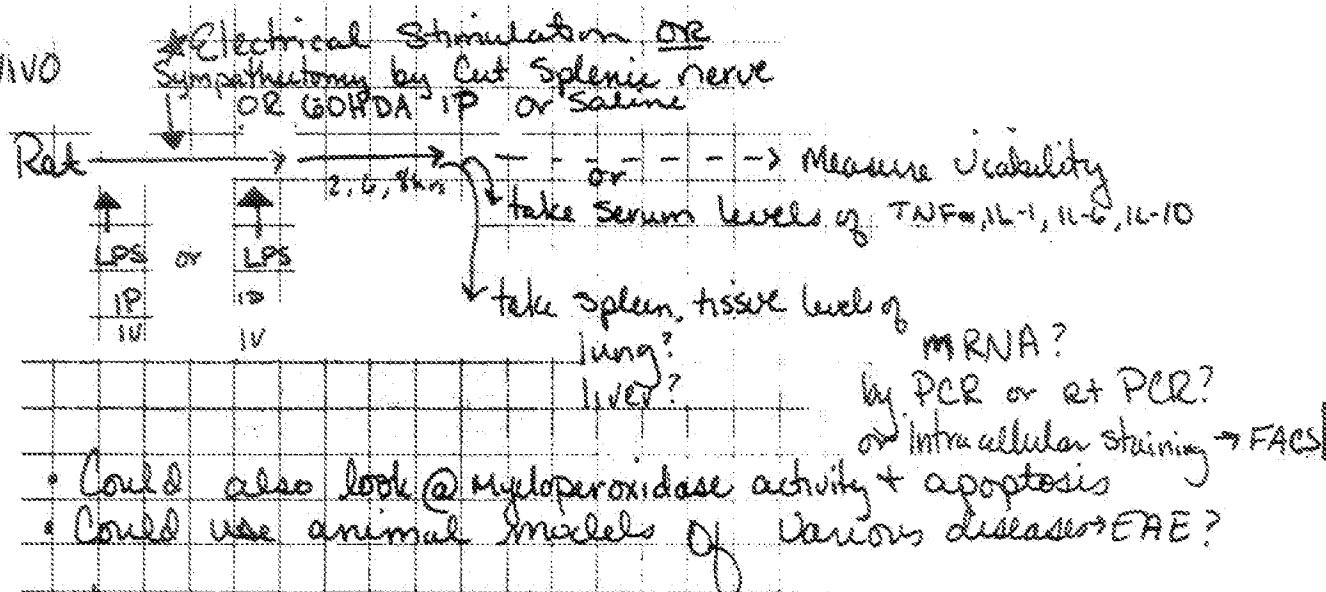
To test *in vitro* / *in vivo* effect of noradrenergic agonists on splenic lymphocyte cytokine following LPS activation; follow w/ *in vivo* splenic stim or Sympathectomy

Experimental Design

IN VITRO



IN VIVO



It would be important to do various stim parameters to determine the effects on immunomodulation

pen (2002) it is feasible that different parameters would produce different outcomes - possibly opposite?

Could be that interacting w/ one type of receptor do thing + the other type (A or B) does the opposite - may a dominant antagonist to the one that produce undesired effect

Electrical Stim to the spleen

Rational:

- No Cholinergic nerve terminal & virtually no afferent supply in the spleen of rats. (Felton, Cohen, & Bellingier each publish in this area)

- Splenic nerve is considered to consist mainly of sympathetic fibers (noradrenergic)

- Sympathectomy sig ↑ the hemorrhage-induced rise in lung TNF in response to hemorrhage (Molina, 2001)

- Stim of β adrenoreceptors in vitro inhibits blastogenic responses of lymphocytes to T & B cell mitogens, IL-2 induced proliferation of lymphocytes, lytic activity of cytotoxic T cells & T cell dependent Ab production

- However, other labs report enhancement in lymphocyte proliferation, lytic activity & antibody responses by β -adrenergic stimulation (Hathfield & M. Sanders)

Suggest a means not for decrease neurotransmitter

serotonins are likely to close response are low levels in β adrenoreceptors lymphocyte prolifer high levels \downarrow lymphocyte prolifer

electrical I Propose:

- * Stimulate w/ implantable device @ the splenic nerve to activate the β receptors on lymphocytes to enhance immune response

to silence sympathetic, may have to do hi frequency?

DC? But, it may not be necessary to silence, on/off immunosuppressor would benefit several diseases.